IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

BLANE NEWMAN, a minor, by and through his father and stepmother and natural guardians, GARY NEWMAN and DEBRA NEWMAN, and MARIAM KHAWAM,	)	**No. 10-CV-01541**
	)	**Magistrate Judge Maria Valdez**
Plaintiffs,	)	
v.	)	
MCNEIL CONSUMER HEALTHCARE, a division of MCNEIL-PPC, INC., and JOHNSON & JOHNSON,	)	
Defendants.		

MEMORANDUM OPINION AND ORDER

This matter is before the Court on Defendants' motion pursuant to Rule 56 of the Federal Rules of Civil Procedure for summary judgment [Doc. No. 121]. The parties have consented to the jurisdiction of the United States Magistrate Judge pursuant to 28 U.S.C. § 636(c). For the reasons set forth below, Defendants' motion is denied.

FACTS[1]

[1] Unless otherwise noted, the following material facts are either undisputed or deemed admitted due to a party's failure to comply with Local Rule 56.1, which this Court

Defendant Johnson & Johnson is a New Jersey Corporation. (LR 56.1(a)(3) ¶ 1.) Defendant McNeil Consumer Healthcare ("McNeil") is a division of McNeil-PPC, Inc., a New Jersey Corporation. (*Id.* ¶ 2.) McNeil manufactures and markets Motrin products. (*Id.*) Motrin is an over-the-counter ("OTC") medication whose active ingredient is ibuprofen, a nonsteroidal anti-inflammatory drug ("NSAID") derived from propionic acid. (*Id.* ¶ 5.) Ibuprofen is widely used to treat pain, inflammation, and fever, with billions of doses sold worldwide. (*Id.*) The Food and Drug Administration ("FDA") approved ibuprofen for adult prescription use in 1974, and for adult OTC use in 1984. (*Id.* ¶ 6.) The FDA approved a prescription version of Children's Motrin in 1989, and approved an OTC version of Children's Motrin in 1995. (*Id.*)

Stevens-Johnson Syndrome ("SJS") is a rare and unpredictable skin disease. (*Id.* ¶ 8.) Toxic Epidermal Necrolysis ("TEN") is even rarer.[2] SJS and TEN are acute, life-threatening conditions involving extensive skin detachment and erosion of the mucosal tissue. (LR 56.1(b)(3)(C) ¶ 1.) TEN is the more severe form, characterized by skin detachment affecting more than thirty percent of the total

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strictly enforces. *See Smith v. Lamz*, 321 F.3d 680, 683 (7th Cir. 2003); *Malec v. Sanford*, 191 F.R.D. 581, 583-84 (N.D. Ill. 2000). The following events are recounted in the light most favorable to the nonmovant, with relevant disputes noted. *See Sow v. Fortville Police Dep't*, 636 F.3d 293, 299–300 (7th Cir. 2011).

[2] The incidence of these diseases is disputed by the parties. For SJS, Defendants reports an estimated incidence of one to six cases per million persons per year from all causes. (LR 56.1(a)(3) ¶ 8.) For TEN, Defendants reports an estimated incidence of .4 to 1.2 cases per million per year from all causes. Plaintiff argues that the actual incidence of SJS and TEN cases is not firmly established, and could be as high as forty-nine to sixty cases per million. (LR 56.1(b)(3)(C)R ¶ 8.)

body surface area. (Id.) Since 1983, McNeil's labeling for its prescription Motrin products has listed SJS as having a "probable causal relationship" with ibuprofen. (*Id.* ¶ 5.) Since 2006, the FDA has required McNeil to expressly state on its prescription Motrin label that "NSAIDs, including Motrin [ ], can cause serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal." (*Id.*) The FDA-approved labels for OTC Motrin and OTC Children's Motrin have never mentioned SJS or TEN or described any diseases or reactions as potentially fatal. (LR 56.1(a)(3)R ¶ 5.)

On February 15, 2005, a Citizen Petition was submitted to the FDA. (LR 56.1(a)(3) ¶ 39.) In it, petitioners requested that a full risk assessment of SJS and TEN associated with ibuprofen be conducted by the FDA; that FDA require the manufacturers of ibuprofen to amplify their prescription and OTC labeling to adequately warn prescribers, health care professionals and consumers of the increased risk of SJS and TEN associated with ibuprofen; and that the FDA require the manufacturers to provide to physicians and consumers instructions to discontinue any/all ibuprofen products at the first sign of a rash, mucosal blisters, or sores in the mouth, eyes, throat, or genitalia, and any unexplained or persistent fever. Citizen Petition to Request Risk Assessment of SJS and TEN at 1-2.

(February 15, 2005) (Hereinafter "Citizen Petition"). The Petition also requested that the FDA withdraw approval of OTC ibuprofen products such as Motrin, and alleged that OTC ibuprofen manufacturers, including McNeil, had misled the FDA in obtaining approval for OTC ibuprofen and its label. (LR 56.1(a)(3) ¶ 41.)

On June 22, 2006, the FDA responded to the Citizen Petition.[3] (*Id.* ¶ 43.) The FDA stated that the agency had "engaged in a comprehensive review of the risks and benefits, including the risks of SJS and TEN, of all approved NSAID products, including ibuprofen. (*Id.*) The FDA also reviewed other available evidence on the incidence of SJS and TEN, "including review of clinical trials submitted to FDA for marketing approvals, review of other clinical studies available in the scientific literature, and review of the Adverse Event Reporting Systems (AERS) surveillance database." (*Id.*) In its response, the FDA concluded that "the overall benefit versus risk profile for ibuprofen products remains very favorable when they are used according to the labeled instructions" and rejected the petitioners' requested that the agency revoke OTC approval of ibuprofen products. (*Id.* ¶ 44.) The FDA refused to require the petitioners' proposed warning, and specifically declined to require that manufacturers include references to SJS and TEN in OTC ibuprofen labels.

[3] Between the time the Citizen Petition was submitted and the FDA responded, the FDA directed all NSAID manufacturers to include new warnings with regard to several potential risks. As pertains to SJS and TEN, the FDA required the labeling for OTC NSAIDs be revised to include a description of early symptoms associated with SJS. (LR 56.1(a)(3) ¶ 38.)

(*Id.* ¶ 47.) The FDA noted that adding easily identifiable references to the symptoms associated with SJS and TEN under the "allergy alert" subheading (e.g., skin reddening, rash and blisters) and a warning that instructed consumers to stop use and seek medical help right away if an allergic reaction occurs would alert and educate consumers about the nature of the allergic reaction associated with SJS and TEN. (*Id.* ¶ 48.)

When the FDA responded to the Citizen Petition, it notes that a search of the U.S. adverse event report database showed that there had been 49 reports of SJS/TEN related to ibuprofen from 1975 through March 2005. (LR 56.1(b)(3)(C) ¶ 32.) The FDA thought that there had been "no notable trend over the years." (*Id.*) Since that time, McNeil has continued to receive adverse event reports ("AERs") regarding ibuprofen-related SJS/TEN cases. (*Id.*) In response to Plaintiffs' discovery request in this case for AERs that McNeil received from 2005 to the present, McNeil produced 117 AERs of ibuprofen-related SJS/TEN cases. (*Id.* ¶ 33.) Eighty-seven of those AERs were received by McNeil prior to June 2009. (*Id.*)

Plaintiffs assert that Mariam Khawam's ("Mariam") and Blane Newman's ("Blane") use of Motrin in the summer of 2009 caused each of them to develop SJS and/or TEN. (*Id.* ¶ 15.) Blane's allegations pertain to OTC Children's Motrin, while Mariam's allegations pertain to OTC Motrin IB; both OTC Children's Motrin and OTC Motrin IB have the same active ingredient and include materially identical

labels.[4] (*Id.*) On June 25, 2009, Mariam's mother gave her a dose of Motrin to treat a fever; Mariam was given at least two more doses that day to treat the fever. (*Id.* ¶ 19.) The next day, Mariam's fever had reached 103.5 degrees, her eyes were bloodshot, and she had lumps in her throat. (*Id.*) Mariam's pediatrician recommended that she continue taking Motrin at double the recommended dosage while her fever remained high. (*Id.* ¶ 20.) Mariam's fever continued to rise and she developed a small rash on her abdomen; on the morning of June 27, Mariam's temperature reached 104 degrees and the rash spread to her arms and back. (*Id.*) By the morning of June 28, Mariam's skin had started to blister. (*Id.* ¶ 21.) She was given another double-dose of Motrin and taken to the Emergency room where she was diagnosed with SJS/TEN. (*Id.*) Mariam has suffered serious and ongoing injuries as a result of the disease. (*Id.*)

On July 6, 2009, Blane's stepmother gave him a dose of Motrin to treat a fever. (*Id.* ¶ 24.) Blane took several more doses of Motrin the next day but remained feverish and continued to feel unwell. (*Id.*) By the afternoon of July 7, Blane's stepmother noted that he had developed reddish bumps on the back of his neck; by that evening, he had more bumps on his back and the bumps spread to Blane's upper body, back, chest, face, arms and neck by July 8. (*Id.*) Blane's stepmother decided to stop giving Blane further doses of Motrin and took him to the doctor's office. (*Id.* ¶ 25.) There, a nurse practitioner diagnosed Blane with a severe reaction

[4] Accordingly, unless stated otherwise, the term "Motrin" will be used to refer to both Children's Motrin and Motrin IB.

to poison ivy and recommended that he continue to take Motrin, along with Benadryl and a steroid. (*Id.*) Blane's symptoms continued to worsen and by July 9, the bumps had turned to blisters, which had spread to other parts of his body. (*Id.* ¶ 26.) Blane's stepmother took him to the emergency room later that day, and the ER doctor who saw Blane suspected SJS and transferred him to Loyola University Medical Center, where he was diagnosed with SJS/TEN. (*Id.*; LR 56.1(b)(3)(C) ¶ 8-9.) Blane has suffered serious and ongoing injuries as a result of the disease. (LR 56.1(a)(3) ¶ 26.)

In June and July of 2009, the label for Motrin provided as follows:

> **WARNINGS:**
>
> ***Allergy Alert***: Ibuprofen may cause a severe allergic reaction, especially in people allergic to aspirin. Symptoms may include:
>
> - hives
> - facial swelling
> - asthma (wheezing)
> - shock
> - skin reddening
> - rash
> - blisters
>
> If an allergic reaction occurs, stop use and seek medical help right away [ ]
>
> ***Stop use and ask a doctor if***
>
> - you feel faint, vomit blood, or have bloody or black stools. These are signs of stomach bleeding.
> - pain gets worse or lasts more than 10 days
> - fever gets worse or lasts more than 3 days
> - stomach pain or upset gets worse or lasts
> - redness or swelling is present in the painful area
> - any new symptoms appear

(*Id.* ¶ 36.) This warning language has not changed in the years since Blane and Mariam consumed Motrin, and these were the warnings on the labels of the products Blane and Mariam used. (*Id.*)

Plaintiffs maintain that Motrin caused Blane's and Mariam's injuries, that the drug was negligently designed, and that it included improper warnings. (*Id.* ¶ 27.) Plaintiffs' Second Amended Complaint ("Complaint") alleges that Motrin's warnings are defective because there was no adequate warning that consumption of the drugs could result in the severe consequences of SJS and/or TEN. (*Id.*) The Complaint also alleges that the warnings and instructions that accompanied the drugs provided inadequate warnings about the degree of the risk of SJS and/or TEN. (*Id.*) Plaintiffs also contend that the label should state the possible consequences of SJS/TEN reactions including, among others, blindness, massive skin loss, burns over large portions of the body, massive scarring, damage to bodily organs, extensive external and internal injuries, and severe and permanent disability. (*Id.* ¶ 27-29.)

DISCUSSION

A. Summary Judgment Standard

Summary judgment is appropriate where "the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving

party is entitled to a judgment as a matter of law." Fed. R. Civ. P. 56(c). The Court must draw all reasonable inferences in favor of the nonmovant. *Bennington v. Caterpillar Inc.,* 275 F.3d 654, 658 (7th Cir. 2001).

However, once the movant has carried its burden under Rule 56(c), "its opponent must do more than simply show that there is some metaphysical doubt as to the material facts." *Matsushita Elec. Indus. Co. v. Zenith Radio Corp.,* 475 U.S. 574, 586 (1986). The party opposing summary judgment must offer admissible evidence in support of his version of events, and hearsay evidence does not create a genuine issue of material fact. *McKenzie v. Ill. Dep't of Transp.,* 92 F.3d 473, 484 (7th Cir. 1996); *see Larimer v. Dayton Hudson Corp.*, 137 F.3d 497, 500 (7th Cir. 1998) ("'If the non-moving party bears the burden of proof on an issue, . . . that party may not rest on the pleadings and must instead show that there is a genuine issue of material fact.'") (citation omitted). "The mere existence of an alleged factual dispute is not sufficient to defeat a summary judgment motion. . . . The nonmovant will successfully oppose summary judgment only when it presents 'definite, competent evidence to rebut the motion.'" *Vukadinovich v. Bd. of Sch. Trs. of N. Newton Sch. Corp.*, 278 F.3d 693, 699 (7th Cir. 2002) (citations omitted).

"In considering a motion for summary judgment, this court is not required to scour the record in search of evidence to defeat the motion; the nonmoving party must identify with reasonable particularity the evidence upon which the party relies." *Pleniceanu v. Brown Printing Co.*, No. 05 C 5675, 2007 WL 781726, at *7 (N.D. Ill. Mar. 12, 2007) (citing *Johnson v. Cambridge Indus., Inc.,* 325 F.3d 892,

898 (7th Cir. 2003)); *see also Estate of Moreland v. Dieter*, 395 F.3d 747, 759 (7th Cir. 2005) ("We will not scour a record to locate evidence supporting a party's legal argument."); *Knapp v. County of Jefferson*, No. 06 CV 4028, 2007 WL 496396, at *1 (S.D. Ill. Feb. 13, 2007) (denying summary judgment where defendant's brief "contains no facts section and . . . fail[s] to point to the relevant portions of the record to establish the facts of this case").

B. Analysis

Defendants argue that Plaintiffs' claims are preempted by federal law. Preemption occurs when state law is invalidated because it conflicts with federal law. *Mason v. Smithkline Beecham Corp.*, 596 F.3d 387, 390 (7th Cir. 2010). The basis for federal preemption is found in the Supremacy Clause of the United States Constitution: "[T]he Laws of the United States . . . shall be the supreme law of the land [.]" U.S. CONST. art. VI, cl. 2. The Supreme Court has identified three forms of preemption: (1) where Congress expressly states its intent to preempt; (2) where Congress's scheme of federal regulation is sufficiently comprehensive to give rise to a reasonable inference that it leaves no room for the state to act; and (3) where state law actually conflicts with federal law. *Cal. Fed. Sav. & Loan Ass'n v. Guerra*, 479 U.S. 272, 280-81 (1987). At issue here is the third instance, conflict preemption, which occurs when (1) "compliance with both state and federal law is impossible," or (2) "when the state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *California v. ARC America Corp.*, 490 U.S. 93, 100-01 (1989) (quotation omitted).

Before addressing the specific preemption claims, it is important to make two observations. First, that the preemption inquiry begins by determining the intent of Congress. *See Medtronic v. Lohr*, 518 U.S. 470, 485-86 (1996). And second, "In all preemption cases, and particularly those in which Congress has legislated in a field which the States have traditionally occupied, we start with the assumption that the historic police powers of the States were not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress." *Wyeth v. Levine*, 129 S. Ct. 1187, 1194-95 (2009).

1. Congressional Intent

In ascertaining the intent of Congress, this Court relies upon the Supreme Court's review of the relevant history of federal regulation of drugs and drug labeling in *Levine*.[5] In 1906, "Congress enacted its first significant public health law, the Federal Food and Drugs Act." *Id.* at 1195. The act, which prohibited the manufacture of adulterated and misbranded drugs, supplemented state regulation and common-law liability. *Id.* In the 1930's, Congress enacted the Federal Food,

[5] In *Levine*, the plaintiff was severely injured when she was injected with the antinausea drug Phenergan via the "IV-push" method of injection. The plaintiff sued the manufacturer of Phenergan for failing to provide an adequate warning about the risks involved with the different methods of administering the drug. The plaintiff won a jury verdict. On appeal, the manufacturer argued that the plaintiff's failure-to-warn claims were preempted because it was impossible for the manufacturer to comply with both state law duties and federal labeling obligations, and that recognition of the plaintiff's state tort action would create an unacceptable obstacle to the accomplishment and execution of the full purposes and objectives of Congress. The Court concluded that the plaintiff's claims were not preempted: the manufacturer failed to demonstrate that it was impossible for it to comply with both federal and state requirements, and that recognition of the plaintiff's state tort inadequate labeling claim did not frustrate the objectives of Congress. *See generally Levine*, 129 S. Ct. at 1187.

Drug, and Cosmetic Act ("FDCA"), which required every manufacturer to submit applications for new drugs. *Id.* "As it enlarged the FDA's powers to protect the public health and assure the safety, effectiveness, and reliability of drugs, Congress took care to preserve state law." *Id.* at 1195-96 (internal citations omitted). The 1962 amendments added a saving clause, "indicating that a provision of state law would only be invalidated upon a 'direct and positive conflict' with the FDCA. Consistent with that provision, state common-law suits continued unabated despite FDA regulation." *Id.* At 1196 (internal citations omitted).

2. Impossibility

The Supreme Court has held that conflict preemption is "a demanding defense." *Id.* at 1199. To prevail, Defendants must "demonstrate that it was impossible for it to comply with both federal and state requirements." *Id.* In the context of preemption of state law claims premised on the inadequacy of a drug label, the Court has held that "[a]bsent *clear evidence* that the FDA would not have approved a change to [a drug's label], we will not conclude that it was impossible for [the manufacturer] to comply with both federal and state requirements." *Id.* at 1198 (emphasis added).

The Court did not clarify what constitutes "clear evidence," but the Seventh Circuit has interpreted and applied the standard in situations relatively similar to the instant case. In *Mason*, the Seventh Circuit explained that the "journey to deciphering the 'clear evidence' standard begins with understanding how drug manufacturers receive approval to market new prescription drugs and to change a

label once it has been approved." 596 F.3d at 391. Before a new drug may be marketed, the manufacturer is required to submit a "New Drug Application" to the FDA. The FDA then must determine whether the application demonstrates by substantial evidence that the drug is efficacious. 21 U.S.C. 355(d)(5). FDA Approval is conditioned on the use of the label it suggests. 21 C.F.R. § 314.105(b). After approval, the FDA continues to have authority over the drug and its label, but the manufacturer has the ability to change the label without prior FDA approval through the "changes being effected" ("CBE") labeling protocol. The CBE regulation allows a manufacturer to modify a label to "add or strengthen a contraindication, warning, precaution, or adverse reaction" or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product" where there is "newly acquired information" about the drug. 21 C.F.R. § 314.70(c)(6)(iii)(A), (C); Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 49063-01, 49069 (Aug. 22, 2008). The manufacturer's ability to make CBE labeling changes "underscores a central premise of federal drug regulation: A 'manufacturer bears responsibility for the content of its label at all times.'" *Mason*, 596 F.3d at 392 (quoting *Levine*, 129 S. Ct. at 1197-98). In other words, once a manufacturer becomes aware of a risk of harm from its drug, it has an independent duty to provide a warning that adequately describes that risk.

Defendants argue that the FDA's 2006 response to the Citizen Petition constitutes clear evidence that the FDA would have prohibited the warning

Plaintiffs say is required, and that therefore, Plaintiffs' failure to warn, negligence and consumer fraud claims are preempted by federal law because – assuming any state law liability – compliance with both federal and state law would be impossible for Defendants. Defendants' conflict preemption defense fails for two distinct reasons.

A. unconsidered warnings

First, in its response to the Citizen Petition, the FDA did not reject the warning Plaintiffs claim is required. Determining what was considered and rejected depends upon what was requested in the Citizen Petition, and how the FDA responded to those requests. In the "Introduction and Action Requested" portion of the Citizen Petition, petitioners requested that the FDA "require the manufacturers of ibuprofen to amplify their . . . OTC labeling to adequately warn . . . consumers of the increased risk of Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) associated with ibuprofen." Citizen Petition at 1. Then, in the "Conclusion and Remedies Sought" section of the Citizen Petition, petitioners requested that the FDA either reconsider OTC status for ibuprofen products, or provide the following labeling changes to OTC ibuprofen products:

> ***Warnings*** **(to follow "Allergy alert")**
> **Serious Skin Reactions:** Ibuprofen may cause serious skin reactions that begin as rashes and blisters on the skin, and in the areas of the eyes, mouth and genitalia. These early symptoms may progress to more serious and potentially life-threatening diseases, including Erythema Multiforme, Stevens Johnson Syndrome and Toxic Epidermal Necrolysis. Seek immediate medical attention if any of these symptoms develop while taking ibuprofen.

> **Stop use and ask a doctor if**
> - a skin rash or blisters on the eyes, mouth or genitalia occur because these symptoms may be an early sign of rare and life-threatening reactions including Erythema Multiforme, Stevens Johnson Syndrome and Toxic Epidermal Necrolysis.

Citizen Petition at 25. The FDA responded to the petitioners' request as follows:

> We agree that the labeling for OTC NSAIDs, including all ibuprofen products, should be improved to warn consumers about the risks of severe skin reactions associated with OTC ibuprofen products. As a result, we have requested that manufacturers include under the Allergy alert subheading the symptoms associated specifically with SJS and TEN. We do not believe that it is useful to include the specific terms *SJS*, *TEN*, or *erythema multiforme*, *Stevens-Johnson Syndrome*, and *toxic epidermal necrolysis* in the OTC label because most consumers are unfamiliar with these terms. In addition, effective OTC labeling communicates warning information in a manner that consumers can quickly and easily identify and understand. Consequently, we believe a description of symptoms is more appropriate. Therefore, prominently displayed under the ***Allergy alert*** subheading in the Drug Facts label, the labeling will include:
>
> - skin reddening
> - rash
> - blisters
>
> In addition, under the ***Allergy alert*** subheading, the labeling will state: "If an allergic reaction occurs, stop use and seek medical help right away." We believe that adding these symptoms to the ***Allergy alert***, with advice to stop use and seek medical attention immediately, will alert and educate consumers to the nature of the allergic reactions associated with SJS and TEN. Further, we intend to continue our consumer education efforts regarding the safe and effective use of OTC pain relievers.

FDA Letter to Roger E. Salisbury, Doc. No. 2005P-0072/CP1, at 8-9 (June 22, 2006) (Hereinafter "FDA Response").

Plaintiffs have not alleged that the OTC Motrin warning label should use the terms "SJS" or "TEN." Plaintiffs have also not alleged that the label should include the phrases "life-threatening diseases," "serious skin reactions," or rashes and blisters around the "eyes, mouth, and genitalia." Instead, part of Plaintiffs' position is that the label is inadequate for not conveying that ibuprofen can cause TEN-related severe and permanent injuries such as massive skin loss, blindness, scarring, and permanent disability. The FDA's reasoning for not including specific references to SJS and TEN was that consumers are unfamiliar with those terms. The FDA's reasoning for including some early symptoms of SJS and TEN was that the agency believed that consumers could quickly and easily identify and understand them. As opposed to terms like SJS and TEN, consumers *are* familiar with injuries like blindness and scarring; and including such information does not seem as if it would keep consumers from quickly and easily understanding the potential severity of an adverse reaction to ibuprofen.

The Citizen Petition did include phrases like "serious skin reactions" and "life-threatening diseases" and the FDA did not ultimately require such language, but the agency provided no reasoning for those particular decisions; therefore, conclusions regarding how those phrases and their alleged analogues were considered and evaluated by the FDA are speculative. Furthermore, those phrases were part of the petitioners' overall warning suggestion that the FDA said that it

rejected because of specific references to diseases that are unknown to most consumers. Put differently, those phrases that are the most similar to Plaintiffs' warnings were not suggested by the petitioners as individual, discrete elements; that the phrases were not included in the FDA's warning is not necessarily a rejection of those particular phrases.

Defendants contend that the Citizen Petition need not have contained all of the precise language Plaintiffs allege should be included, and that if the FDA had to reject every possible formulation of a particular warning, there could never be preemption. Defendants explain that requiring the FDA to expressly reject references to the more serious consequences of SJS and TEN would impose an unreasonable burden on the FDA. Defendants maintain that such a requirement would have required the FDA to respond to every point in the Petition's 30-some pages and to parse the language in the petition's proposed warnings and explain why the FDA was (or was not) accepting every particular word or phrase. Defendants are right that the FDA should not have to reject every possible formulation of a particular warning in order for there to be clear evidence of rejection. Here, however, the FDA's response does not even address the petitioners' references to the more serious consequences of SJS and TEN.

Also, the Court is certainly not requiring that the FDA respond to "every point in the Petitioner's 30-some pages" in order for there to be clear evidence of preemption in some cases; instead, the focus of the FDA's response (here, and in most cases) concerns the Citizen Petition's requested remedies, and more

specifically – in petitions alleging inadequate labeling – the petitioners' proposed label. For there to be "clear evidence" of rejection, it may be necessary in some instances for the FDA to parse the language in a petition's explicit requests and explain why particular requests are appropriate and others are not.[6] Otherwise, it may be impossible to determine what the agency is rejecting. Finally, it remains the case that the FDA never need burden itself by responding to each and every point in a petition or proposed warning; the only consequence is that there may not be preemption in a case concerning that warning.

Seemingly complicating matters is the Defendants' persistent reliance on *Robinson v. McNeil Consumer Healthcare*, 615 F.3d 861 (7th Cir. 2010). *Robinson* involved the same drug, the same injuries, the same manufacturer, and much of the same evidence, and Defendants maintain that in *Robinson* the Seventh Circuit has already suggested that there is preemption in exactly these circumstances. Defendants' reliance is misplaced. In *Robinson*, the court cited the clear evidence standard "as one reason of several to uphold the lower court's refusal to allow the plaintiff, on the eve of trial, to add a breach of implied warranty claim." *Schedin v. Ortho-McNeil-Janssen Pharm., Inc.*, No. 08-5743, 2011 WL 834020, at *5 (D. Minn. Mar. 4, 2011) (citing *Robinson*, 615 F.3d at 872-73). Even if the court's statement

[6] In other instances, however, the FDA may reject a whole series of warnings without concerning itself with various formulations. For example, by rejecting references to SJS and TEN and explaining its reasoning for doing so, the agency has likely established clear evidence that it would have rejected *any* proposed warnings containing references to SJS and TEN.

could be considered a holding that the plaintiff's claims were preempted, however, the court's explanation of the "clear evidence" in the case was limited to the FDA's refusal to require *references to SJS and TEN* on the warning label for OTC ibuprofen products. *Id.* at 873. As is mentioned above, Plaintiffs are not alleging that the OTC Motrin warning label should use the terms "SJS" or "TEN."[7]

Further, Plaintiffs argue that their claims are not preempted because the FDA's Response, while *refusing to require* the warning proposed by the Citizen Petition, did not *prohibit* additional warnings and only established minimum requirements for the manufacturer. In other words, Plaintiff asserts that until an ibuprofen manufacturer unilaterally proposes warnings about the severe injuries caused by ibuprofen-induced TEN and the FDA prohibits such a warning, there can be no impossibility preemption. While the holding of *Levine* is not directly on point, the context of that case seems to support the Plaintiffs' argument. *Levine*, 129 S. Ct. at 1198. Defendants', on the other hand, claim that *Robinson* implicitly forecloses Plaintiffs' position. But this argument is less than compelling because of the aforementioned problems with reliance on that case in this circumstance. The federal courts have not squarely addressed the issue;[8] but had Defendant McNeil

[7] It is also worth noting that, in *Robinson*, the plaintiff used ibuprofen and suffered her injuries in September of 2005, nine months *before* the FDA Responded to the Citizen Petition. There was no question as to whether the FDA would have refused to require plaintiff's suggested warnings; the FDA Response made that clear. Here, we are confronted with a different set of facts: Blane and Mariam suffered their injuries *three years after* the FDA Response. The Court addresses the relevancy of this temporal gap below.

[8] Defendants do cite a California Supreme Court case that held that the FDA's response to a citizen petition "established a federal policy prohibiting defendants from

added the warnings suggested by Plaintiffs (or similar warnings), it is unlikely that such new content would have rendered the Motrin products "misbranded": "The FDCA does not provide that a drug is misbranded simply because the manufacturer has altered an FDA-approved label; instead, the misbranding provision focuses on the substance of the label and, among other things, proscribes labels that fail to include 'adequate warnings.'" *Levine*, 129 S. Ct. at 1197 (quoting 21 U.S.C. § 352(f)). And, as the Supreme Court notes, "the very idea that the FDA would bring an enforcement action against a manufacturer for strengthening a warning pursuant to the CBE regulation is difficult to accept – neither [the manufacturer] nor the United States has identified a case in which the FDA has done so." *Id.* Similarly, Defendants have not identified such a case.[9]

B. newly acquired evidence

The second reason Defendants fail to establish impossibility is that the FDA's 2006 response to the Citizen Petition is not clear evidence that the FDA would have prohibited *in 2009* the warning Plaintiffs allege is required. It is undisputed that during the three years after the FDA's search and evaluation of the U.S. adverse event report database, a significant number of AERs of ibuprofen-related SJS and

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giving consumers any warning other than the one approved by the FDA." *Dowhal v. Smithkline Beecham Corp.*, 88 P.3d 1, 11 (Cal. 2004). Obviously, however, that case was decided before *Levine*.

[9] It is unnecessary to determine whether the FDA's refusal to require a warning can constitute prohibition (and whether it does in this case) since this Court has determined that the Plaintiffs' claims are not preempted for other reasons.

TEN cases have accumulated; and it is also undisputed that new information can undermine an earlier FDA determination.

In *Levine*, the Supreme Court explained that the "newly acquired information" language of the amendment to the CBE regulation includes new data, and "also encompasses 'new analyses of previously submitted data.'" 129 S. Ct. at 1197 (quoting 73 Fed. Reg. 49603-01, 49604). The Court explained that

> [t]he rule accounts for the fact that risk information accumulates over time and that the same data may take on a different meaning in light of subsequent developments: "[I]f the sponsor submits adverse event information to FDA, and then later conducts a new analysis of data showing risks of a different type or of greater severity or frequency than did reports previously submitted to FDA, the sponsor meets the requirement for 'newly acquired information."

Id. (quoting 73 Fed. Reg. 49603-01, 49603-07). In that case, the Court admitted that the record was limited concerning what newly acquired information the defendant manufacturer had or should have had about the risks of its drug, Phenergan. *Id.* The plaintiff did, however, present evidence of 20 incidents prior to her injury in which a Phenergan injection resulted in gangrene and an amputation. *Id.* After the first such incident came to [the manufacturer's] attention in 1967, it notified the FDA and worked with the agency to change Phenergan's label; "[i]n later years, as amputations continued to occur, [the Manufacturer] could have analyzed the accumulating data and added a stronger warning." *Id.*

In this case, when the FDA responded to the Citizen Petition, it noted that a search of the U.S. adverse event report database showed that there had been forty-

nine reports of SJS/TEN cases related to ibuprofen from 1975 through March 2005. *See* FDA Response at 4. The FDA stated that there was "no noticeable trend over the years in [the] reporting of adverse events given the small number of reports received per year." *Id.* Since that time, however, Defendant McNeil has continued to receive AERs regarding ibuprofen-related SJS and TEN cases, (LR 56.1(b)(3)(C) ¶ 32), and has produced to Plaintiff 117 AERs of ibuprofen-related SJS and TEN cases. (*Id.* ¶ 33.) Eighty-seven of those AERs were received by McNeil prior to the time when Blane and Mariam suffered TEN-related injuries after using Motrin products. (*Id.*) Similar to the manufacturer in *Levine*, McNeil could have – and Plaintiffs argue *should* have – evaluated the new data, and/or analyzed the overall data and added a stronger warning; and because of the new data, the FDA's Response can no longer be treated as clear evidence that the agency would not have approved a change to the Motrin labels.

Defendants assert that while new information can undermine an earlier FDA determination, the new information must be material and must make it more likely that the FDA would approve a new warning. Defendants maintain since the FDA was aware of "some" AERs when it responded to the Citizen Petition, there is no reason to think the existence of additional AERs would have changed its conclusion. Defendants provide little, if any, reasoning to support this claim. In the FDA's response, the agency states that its "analysis of AERS and other data indicates that

the risk is not as great as [petitioners] assert in the petition." FDA Response at 5.[10] That is, the FDA relied, at least in part, on its analysis of AERs to determine the SJS and TEN risks associated with ibuprofen use. Newly acquired information – data yet to be evaluated by the FDA – shows that while there were forty-nine reports of SJS/TEN related to ibuprofen from 1975 through March 2005 (a thirty-year span), there were eighty-seven such AERs from 2005 through 2009. Considering the FDA's use of the information contained in the older AERs, it seems likely that the new information might change the FDA's analysis.[11]

Defendants also argue that it is "well established" that case reports are not reliable scientific evidence of causation. Defendants point to no court in this Circuit that has held as such, and even if the cases Defendants cite are accorded significant deference, Defendants have confused "sufficient evidence of a causal association" (what is required under the CBE regulation) with definitive evidence of causation.[12]

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[10] On another occasion in its Response, the Agency states that they "believe that the available evidence, including but not limited to adverse events reports, indicates that the incidence of SJS and TEN is less than the cited estimate of 6 or 7 cases per 100,000." FDA Response at 3.

[11] On its website, the FDA explains that "[p]otential signals of serious risks are normally based upon groups of AERS reports, although a single AERS report could lead to further evaluation of a potential safety issue. *Potential Signals of Serious Risks / New Safety Information Identified from the Adverse Event Reporting System (AERS)*, FOOD AND DRUG ADMINISTRATION, http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/surveillance/adversedrugeffects/ucm082196.htm (last updated September 21, 2011).

[12] The cases upon which Defendants rely illustrate this confusion. In *Casey v. Ohio Med. Prod's*, 877 F. Supp. 1380 (N.D. Cal. 1995), the court determined that the opinion of a witness solely based on very few case reports was not based on reliable scientific evidence and was not admissible under *Daubert*. *Id.* at 1385. According to that court, such case reports are not reliable scientific evidence of causation "because they simply describe[ ]

The regulations promulgated by the FDA explicitly state that "labeling must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a *causal association* with a drug; *a causal relationship need not have been definitely established*." 21 C.F.R. 201.57 (*cited as the appropriate standard in* 73 Fed. Reg. 49603-01, 49604) (emphasis added). In other words, so long as the information in the new AERs yields reasonable evidence of a stronger causal association, then the reports constitute newly acquired evidence that may very well affect the FDA's analysis. Furthermore, regardless of Defendants' characterization of AERs, it is plain that the FDA has made the decision to rely on them and utilize them in its determinations. In its response to the Citizen Petition, the agency explained that it "uses a number of methods to monitor the safety of marketed drugs, including review of clinical trials . . . review of other clinical studies . . . and review of the Adverse Event Reporting System surveillance

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reported phenomena without comparison to the rate at which the phenomena occur in the general population or in a defined control group; do not isolate and exclude potentially alternative causes; and do not investigate or explain the mechanism of causation." *Id.* at 1385. In *Rider v. Sandoz Pharm. Corp.*, 295 F.3d 1194 (11th Cir. 2002), the court held that while they may support other proof of causation, case reports alone ordinarily cannot prove causation." *Id.* at 1199. The court noted that courts have to consider that "case reports are merely accounts of medical events. They reflect only reported data, not scientific methodology." *Id.* Defendants ignore that AERs are handled in a specific manner by clinical experts at the FDA, that AERs are evaluated alongside other information, that further evaluation (*e.g.* epidemiological studies) might be conducted if reports identify a potential safety concern, and that the FDA understands and anticipates the limitations of AERs. *See Adverse Event Reporting System (AERS)*, FOOD AND DRUG ADMINISTRATION, http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/surveillance/adversedrugeffects/default.htm (last updated Aug. 20, 2009); *see also* FDA Response at 2-4.

database implemented in 1997." FDA Response at 2. On its website, the FDA states that the Adverse Event Reporting System is

> [A] useful tool for FDA, which uses it for activities such as looking for new safety concerns that might be related to a marketed product, evaluating a manufacturer's compliance to reporting regulations and responding to outside requests for information. The reports . . . are evaluated by clinical reviewers in the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) to monitor the safety of products after they are approved by FDA. If a potential safety concern is identified . . . further evaluation might include epidemiological studies.

Adverse Event Reporting System (AERS), FOOD AND DRUG ADMINISTRATION, http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/surveillance/adversedrugeffects/default.htm (last updated Aug. 20, 2009). Because of the importance of AERs to the FDA's evaluation process, AERs may constitute newly acquired evidence.

The Seventh Circuit's decision in *Mason v. Smithkline Beecham Corporation* supports this conclusion. There, the court explained that a "temporal gap" of several years is "especially important in the analysis of prescription[13] drugs because it constantly evolves as new data emerges." *Mason*, 596 F.3d at 395. In *Mason*, the plaintiffs' 23-year-old daughter Tricia committed suicide in March of 2003, two days after starting Paxil. *Id.* at 389. The court recognized that the FDA had a long history of considering whether a suicide warning should be placed on the labels of a

[13] This Court sees no reason to distinguish between prescription drugs and OTC drugs in this particular context.

class of prescription antidepressants known as selective serotonin re-uptake inhibitors (SSRIs). *Id.* at 393-95. The court acknowledged that the FDA had rejected a citizen petition to change the label for the SSRI Prozac to include a warning about suicide "several years" before Tricia's death and stated that the gap between the FDA's rejection and the suicide was "especially important." *Id.* at 395.

Defendants distinguish *Mason* by explaining that the FDA's rejection of the citizen petition was accompanied by a "call to do more research," and that the court discounted the significance of the administrative history of the SSRI Prozac because the case actually dealt with the different (albeit similar) SSRI Paxil. *Id.* Neither of Defendants' points changes the fact that, in an analytical environment where there is constant evolution, a lot can change in three years. In this case, there has been a clear and significant increase in the number of relevant AERs after the FDA's Response. This newly acquired information yields the conclusion that even if there was clear evidence that the FDA would not have approved a change to the Motrin labels at some point in the past, such evidence is no longer sufficiently obvious for preemption purposes.

3. Frustration of the Purposes of Congress

Defendants also argue that some of Plaintiffs' claims are preempted because Plaintiffs' success on those claims would frustrate the accomplishment and execution of the full purposes and objectives of Congress. The argument is that since Plaintiffs' design defect and warranty claims are premised on the allegation that OTC ibuprofen is "unreasonably dangerous" and should not be sold on the OTC

market, they are in conflict with the FDA's determination that ibuprofen's risk/benefit profile is "very favorable" and that it is in the "interest of the public health" for it to remain on the OTC market. Plaintiff responds by arguing that Congress explicitly exempted state product liability law when it passed legislation requiring national uniformity for nonprescription drugs. *See* 21 U.S.C. § 379r(e). Furthermore, in *Levine*, the Supreme Court rejected the contention that the FDCA establishes both a floor and a ceiling for drug regulation, and held that Congress intended the FDCA to supplement or bolster consumer protection against harmful products. 129 S. Ct. at 1199. The Court's reasoning is explicit:

> In keeping with Congress' decision not to pre-empt common-law tort suits, it appears that the FDA traditionally regarded state law as a complementary form of drug regulation. The FDA has limited resources to monitor the 11,000 drugs on the market, and manufacturers have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge. State tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly. They also serve a distinct compensatory function that may motivate injured persons to come forward with information. . . . Thus, the FDA long maintained that state law offers an additional, and important, layer of consumer protection that complements FDA regulation.

Id. at 1202.

Defendants assert that *Levine* is inapplicable since it involved a failure-to-warn claim, not a design defect or warranty claim. Defendants contend that while simultaneously complying with both federal and state warning requirements will pose little difficulty in most cases, design defect and warranty claims can limit the

availability of drugs that the FDA has determined to be safe. In support of its position, Defendants quote a specific portion of *Abbot v. Am. Cyanamid Co.*, 844 F.2d 1108 (4th Cir. 1988): "The overall goal of the PHSA and FDCA is the safety of drugs and biologic products. That goal is more enhanced than frustrated by state law. *However, the federal government has favored not only vaccine safety but also availability and use . . . [which] can be frustrated by state tort law*." *Id.* at 1113 (emphasis added). The Defendants have cherry-picked from the *Abbot* decision. The remaining portion of the decision holds that state tort remedies for allegedly defective vaccines are *not* preempted by federal law. The court noted that "[t]he issue . . . is whether the federal interest requires that federal regulation be viewed as having struck the balance between safety and quantity or whether the regulations merely establish minimum safety standards and allow state regulation to establish the balance. *Id.* The court interpreted the Childhood Vaccine Injury Act of 1986 in order to determine the federal interest and concluded that the legislative history make clear that the act's no-fault compensation program was merely an alternative to, and not a replacement of, state tort recoveries, and that Congress acted with the understanding that state tort remedies were available and that they would continue to be available. *Id.* Similarly, *Levine*'s analysis of the FDCA makes clear that "Congress did not intend FDA oversight to be the exclusive means of ensuring drug safety and effectiveness." 129 S. Ct. at 1200. In fact, the Court found "no merit" in the argument that state tort inadequate labeling claims interfered

with Congress's purpose to entrust an expert agency to make drug labeling decisions that strike a balance between competing objectives. *Id.* at 1199.

Additionally, several courts have held that while the decision in *Levine* was made in the context of a failure-to-warn action, its holding applies equally to design defect claims. *See, e.g.*, *Wimbush v. Wyeth*, 619 F.3d 632 (6th Cir. 2010); *Bartlett v. Mutual Pharm. Co.*, 760 F. Supp. 2d 220 (D.N.H. 2011); *In re Fosamax Prods. Liability Litig.*, 742 F. Supp. 2d 460 (S.D.N.Y. 2010). In *Wimbush*, the defendant sought to distinguish *Levine* on the basis that *Levine* involved an inadequate warning claim whereas the plaintiff's claim was a negligent-bringing-to-market claim. The Court of Appeals explained that the defendant's attempt to distinguish the cases simply pointed to a "distinction without a difference":

> Just as state tort law on adequacy of warnings can be seen as 'complementary' to the FDA's labeling regulation, so too can state law duties regarding the decision to bring a product to market be seen as complementary to the FDA's function of approving a drug for market. This makes sense, as whether the FDA approves a drug for market depends, in very large part, upon the results of the manufacturer's investigation and testing prior to seeking FDA approval. If the manufacturer is negligent in this investigation, then the entire FDA approval process is tainted from the outset. . . . Finally, the overwhelming take-away from the Levine majority opinion is that state tort law has historically played a substantial role in the regulation of drug manufacturers and that Congress has never indicated an intent to change this role.

Id. at 645, n.7. This Court agrees that *Levine*'s logic may reasonably be extended to design defect and warranty claims.

Defendants argue that even if *Levine* is applicable to Plaintiffs' design defect and warranty claims, an actual conflict is still present and there is "clear evidence" that the FDA desires the drug to be available as an OTC product: in the FDA's Response, the agency expressed a clear interest in maintaining "in the pediatric OTC market a range of therapeutic options for the short-term relief of pain." FDA Response at 9. As is explained above, that newly acquired information could undermine the FDA's decisions makes this Court unable to conclude that there is clear evidence that the FDA's 2006 determinations regarding OTC Motrin's risk/benefit profile would have been the same at the time of Plaintiffs' injuries.

4. No Duty to Warn of Idiosyncratic Risks

Defendants, in a footnote, claim that Plaintiffs' failure to warn claim fails for the additional reason that there is no duty to warn of idiosyncratic risks. *Presbrey v. Gillette Co.*, 105 N.E.2d 513, 519-20 (1982). Defendants note that SJS and TEN are exceedingly rare diseases with unknown causes, and that recent studies show that there is no statistically significant correlation between the disease and the use of ibuprofen. Defendants misapply *Presbrey*.

In *Presby*, the court held that "[t]he unusual susceptibility of the consumer is generally recognized as a complete defense where the manufacturer did not know and had no reason to know that a very few users of his product might be injured." *Id.* at 520. Here, it is undisputed that since 1983, McNeil's labeling for its prescription Motrin products has listed SJS as having a "probable causal relationship" with ibuprofen, (LR 56.1(b)(3)(C) ¶ 5), and the FDA has clearly stated

that "NSAIDs, including ibuprofen, are known to cause SJS and TEN." FDA Response at 1. Obviously, McNeil knew that users of its product might be injured; therefore even if there is "unusual susceptibility" in this case, it is not a complete defense to Plaintiffs' failure to warn claim.

CONCLUSION

For the reasons stated above, there is no preemption of Plaintiffs' claims. The Court cannot, as a matter of law, determine either that it was impossible for Defendants to comply with both federal and state requirements simultaneously, or that recognition of Plaintiffs' state law claims will frustrate the objectives of Congress. Therefore, Defendant Clark is not entitled to a grant of summary judgment. Defendant's Motion for Summary judgment [Doc. No. 121] is denied.

SO ORDERED.

ENTERED:

Maria Valdez

DATE: January 9, 2012

HON. MARIA VALDEZ

United States Magistrate Judge